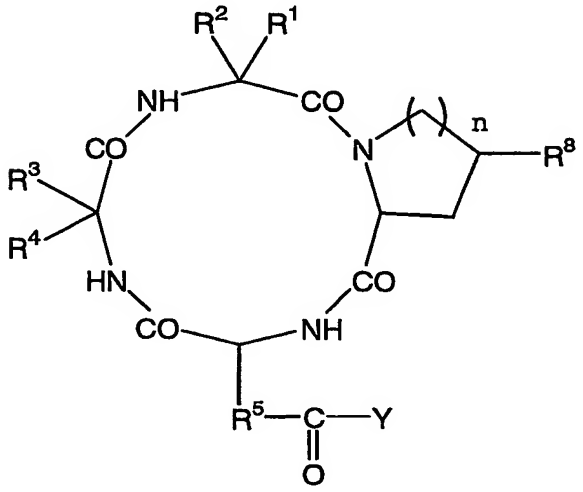
CLAIMS

1. A cyclic tetrapeptide compound of the formula (I):



(I)

wherein

R^1 is hydrogen,

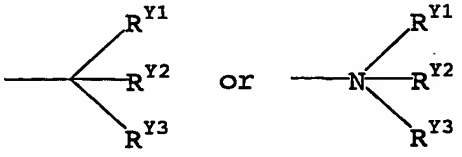
R^2 is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or arylcarbamoyl(lower)alkyl,

R^3 and R^4 are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

R^3 and R^4 are linked together to form lower alkylene or condensed ring, or one of R^3 and R^4 is linked to the adjacent nitrogen atom to form a ring,

R^5 is lower alkylene or lower alkenylene,

Y is



[wherein R^{Y1} is hydrogen, halogen or optionally protected hydroxy,

R^{Y2} is hydrogen, halogen, lower alkyl or phenyl, and

R^{Y3} is hydrogen or lower alkyl],

R^8 is hydrogen or lower alkyl, and

n is an integer of 1 or 2,

providing that,

when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene, R^8 is hydrogen, n is 1, R^{Y1} is optionally substituted hydroxy, R^{Y2} is methyl and R^{Y3} is hydrogen, then R^2 is not unsubstituted benzyl,

or a salt thereof.

2. The cyclic tetrapeptide compound of claim 1, wherein

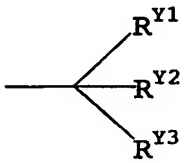
R^2 is phenylcarbamoyl(lower)alkyl; lower alkylcarbamoyl(lower)alkyl; or phenyl(lower)alkyl optionally substituted with one or more suitable substituent(s) selected from the group consisting of lower alkyl, halo(lower)alkyl, lower alkoxy, ar(lower)alkoxy, cyano, hydroxy, halogen, amino, lower alkanoylamino, lower alkylsulfonylamino, aryl, cyclo(lower)alkyloxy, carboxy(lower)alkoxy, heterocyclic(lower)alkoxy, lower alkenyloxy, hydroxy(lower)alkyl, arylcarbamoyl, heterocycliccarbonyl, lower(alkyl)carbamoyl(lower)alkoxy, arylcarbamoyl(lower)alkoxy, lower(alkyl)carbamoyl(lower)alkyl, heterocyclic group, lower alkoxycarbonyl, lower alkoxycarbonyl(lower)alkoxy, lower alkylcarbamoyl, heterocycliccarbonyl(lower)alkyl, heterocycliccarbonyl(lower)alkoxy, aryl(lower)alkoxy and phenylcarbamoyl(lower)alkyl,

R^3 is hydrogen or lower alkyl,

R^4 is lower alkyl or phenyl(lower)alkyl substituted with lower alkoxy,

R^5 is lower alkylene,

Y is



[wherein R^{Y1} is hydrogen or hydroxy, R^{Y2} is halogen or lower alkyl and R^{Y3} is hydrogen] and

R^8 is hydrogen or lower alkyl.

3. The cyclic tetrapeptide compound of claim 2, wherein

R^2 is phenyl(lower)alkyl substituted with a substituent selected from the

group consisting of lower alkyl, halo(lower)alkyl, lower alkoxy, phenyl(lower)alkyloxy, cyano, hydroxy, halogen, amino, lower alkanoylamino, (lower)alkylsulfonylamino, phenyl, cyclo(lower)alkyloxy, carboxy(lower)alkyloxy, pyridyl(lower)alkyloxy, lower alkenyloxy, hydroxy(lower)alkyl, phenylcarbamoyl, piperidinocarbonyl, lower(alkyl)carbamoyl(lower)alkoxy, phenylcarbamoyl(lower)alkoxy, lower(alkyl)carbamoyl(lower)alkyl, pyridyl, lower alkoxycarbonyl, lower alkoxycarbonyl(lower)alkoxy, lower alkylcarbamoyl, morpholinocarbonyl(lower)alkyl, piperidinocarbonyl(lower)alkoxy, phenyl(lower)alkoxy and phenylcarbamoyl(lower)alkyl,

R^3 is lower alkyl,

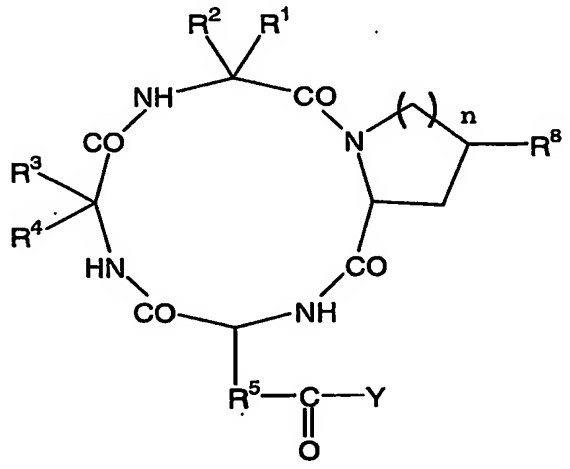
R^4 is lower alkyl, and

R^5 is lower alkylene.

4. A pharmaceutical composition containing the cyclic tetrapeptide compound of any of claims 1 to 3 as an active ingredient, in association with a pharmaceutically acceptable, substantially non-toxic carrier or excipient.

5. The cyclic tetrapeptide compound of any of claims 1 to 3 for use as a medicament.

6. A histone deacetylase inhibitor comprising a cyclic tetrapeptide compound of the formula (I):



(I)

wherein

R^1 is hydrogen,

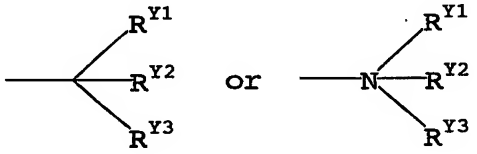
R^2 is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or arylcarbamoyl(lower)alkyl,

R^3 and R^4 are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

R^3 and R^4 are linked together to form lower alkylene or condensed ring, or one of R^3 and R^4 is linked to the adjacent nitrogen atom to form a ring,

R^5 is lower alkylene or lower alkenylene,

Y is



[wherein R^{Y1} is hydrogen, halogen, optionally protected hydroxy

R^{Y2} is hydrogen, halogen, lower alkyl or phenyl, and

R^{Y3} is hydrogen or lower alkyl],

R^8 is hydrogen or lower alkyl, and

n is an integer of 1 or 2,

providing that,

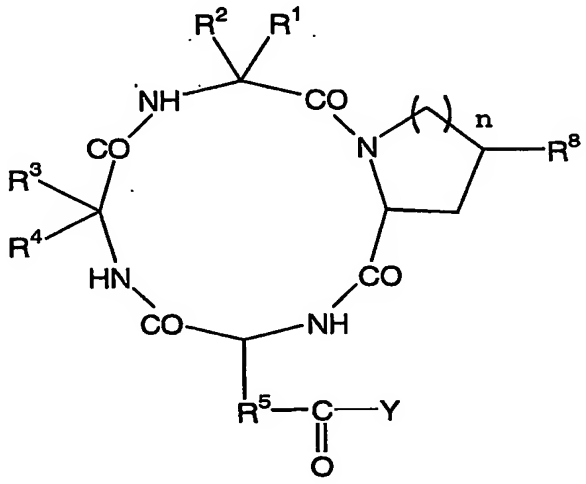
when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene, R^{Y1} is optionally substituted hydroxy, R^{Y2} is methyl and R^{Y3} is hydrogen, then R^2 is not unsubstituted benzyl,

or a salt thereof.

7. A method for inhibiting histone deacetylase, comprising using a cyclic tetrapeptide compound (I) of claim 6.

8. Use of a cyclic tetrapeptide compound (I) of claim 6 for the manufacture of a medicament for inhibiting histone deacetylase.

9. A pharmaceutical composition for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which comprises, as an active ingredient, a cyclic tetrapeptide compound of the formula (I):



(I)

wherein

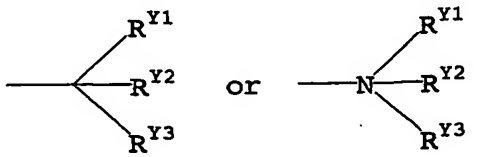
R^1 is hydrogen,

R^2 is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or arylcarbamoyl(lower)alkyl,

R^3 and R^4 are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

R^3 and R^4 are linked together to form lower alkylene or condensed ring, or one of R^3 and R^4 is linked to the adjacent nitrogen atom to form a ring,

R^5 is lower alkylene or lower alkenylene,



Y is

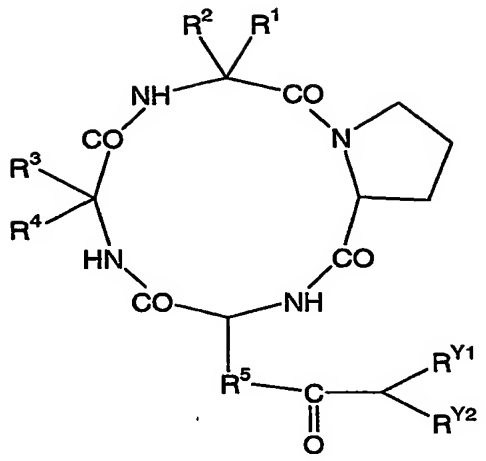
[wherein R^{Y1} is hydrogen, halogen, optionally protected hydroxy
R^{Y2} is hydrogen, halogen, lower alkyl or phenyl, and
R^{Y3} is hydrogen or lower alkyl],
R^8 is hydrogen or lower alkyl, and
n is an integer of 1 or 2,
providing that,
when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene, R^{Y1} is optionally substituted hydroxy, R^{Y2} is methyl and R^{Y3} is hydrogen, then R^2 is not unsubstituted benzyl,
or a salt thereof.

10. A method for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which comprises administering an effective amount of the cyclic tetrapeptide compound (I) of claim 1 to a human being or an animal.

11. Use of the cyclic tetrapeptide compound (I) of claim 1 for the manufacture of a medicament for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.

12. A commercial package comprising the pharmaceutical composition of claim 9 and a written matter associated therewith, the written matter stating that the pharmaceutical composition may or should be used for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.

13. A cyclic tetrapeptide compound of the formula (I'):



(I')

wherein

R^1 is hydrogen,

R^2 is ar(lower)alkyl optionally substituted with one or more suitable substituent(s),

R^3 and R^4 are each hydrogen or lower alkyl, or

R^3 and R^4 are linked together to form lower alkylene,

R^5 is lower alkylene or lower alkenylene,

R^{Y1} is optionally protected hydroxy, and

R^{Y2} is lower alkyl,

providing that,

when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene, R^{Y1} is optionally substituted hydroxy and R^{Y2} is methyl, then R^2 is not unsubstituted benzyl, or a salt thereof.

14. The cyclic tetrapeptide compound of claim 13, wherein

R^2 is phenyl(lower)alkyl optionally substituted with one or more suitable substituent(s) selected from the group consisting of lower alkoxy, ar(lower)alkyloxy, cyano, hydroxy and halogen,

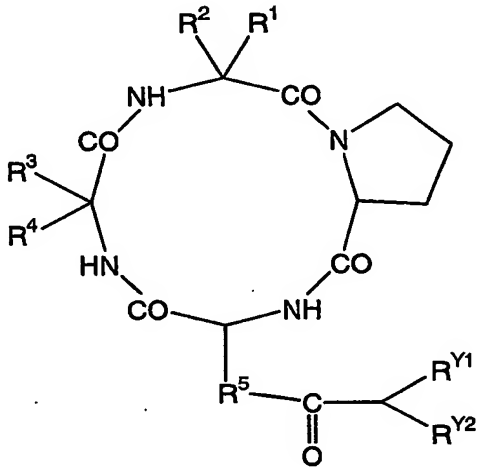
R^3 and R^4 are each lower alkyl, and

R^5 is lower alkylene.

15. A pharmaceutical composition containing the cyclic tetrapeptide compound of claim 13 or 14 as an active ingredient, in association with a pharmaceutically acceptable, substantially non-toxic carrier or excipient.

16. The cyclic tetrapeptide compound of claim 13 or 14 for use as a medicament.

17. A histone deacetylase inhibitor comprising a cyclic tetrapeptide compound of the formula (I'):



(I')

wherein

R^1 is hydrogen,

R^2 is ar(lower)alkyl optionally substituted with one or more suitable substituent(s),

R^3 and R^4 are each hydrogen or lower alkyl, or

R^3 and R^4 are linked together to form lower alkylene,

R^5 is lower alkylene or lower alkenylene,

R^{Y1} is optionally protected hydroxy, and

R^{Y2} is lower alkyl,

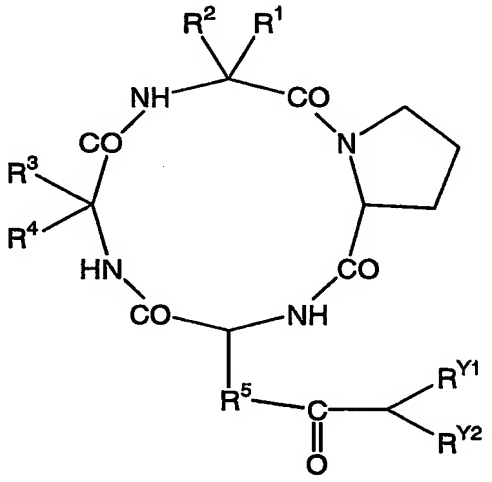
providing that,

when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene, R^{Y1} is optionally substituted hydroxy and R^{Y2} is methyl, then R^2 is not unsubstituted benzyl, or a salt thereof.

18. A method for inhibiting histone deacetylase, comprising using a cyclic tetrapeptide compound (I') of claim 17.

19. Use of a cyclic tetrapeptide compound (I') of claim 17 for the manufacture of a medicament for inhibiting histone deacetylase.

20. A pharmaceutical composition for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which comprises, as an active ingredient, a cyclic tetrapeptide compound of the formula (I'):



(I')

wherein

R^1 is hydrogen,

R^2 is ar(lower)alkyl optionally substituted with one or more suitable substituent(s),

R^3 and R^4 are each hydrogen or lower alkyl, or

R^3 and R^4 are linked together to form lower alkylene,

R^5 is lower alkylene or lower alkenylene,

R^{Y1} is optionally protected hydroxy, and

R^{Y2} is lower alkyl,

providing that,

when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene, R^{Y1} is optionally substituted hydroxy and R^{Y2} is methyl, then R^2 is not unsubstituted benzyl,

or a salt thereof.

21. A method for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which comprises

administering an effective amount of the cyclic tetrapeptide compound (I') of claim 13 to a human being or an animal.

22. Use of the cyclic tetrapeptide compound (I') of claim 13 for the manufacture of a medicament for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.

23. A commercial package comprising the pharmaceutical composition of claim 20 and a written matter associated therewith, the written matter stating that the pharmaceutical composition may or should be used for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.